THE MECHANISMS OF MOTOR AND SENSORY NERVE DYSFUNCTION AFTER CHRONIC ARSENIC EXPOSURE IN RATS

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Background and Aims: Tens of millions of people are exposed to arsenic contaminated drinking water all over the world, including residents in Argentina, Bangladesh, Chile, China, Mongolia, Taiwan, etc. Previous studies have shown that chronic arsenic exposure could cause various cancers, skin diseases, neurological diseases, cardiovascular diseases and cerebrovascular diseases. Recent epidemiologic studies from Bangladesh showed that chronic arsenic exposure was associated with abnormal sensory nerve action potentials. We therefore set up an animal model to explore the mechanisms of neuropathy caused by chronic arsenic exposure.

Methods: We treated spontaneous hypertensive-prone rats with drinking water containing 133 μg/ml of arsenic (experimental group) for 40 consecutive weeks and compared them to a blank control group. At the end of exposure, we assessed motor functions by observing spontaneous locomotor behaviors (including motion distance and motion velocity) in the open field and monitored the sensory function by measuring the pain stimulation latency during the hot plate test. The enzymatic Na(+)/K(+)-ATPase activity of sciatic nerve was determined by a colorimetric assay, and the pathological changes and severity of neuropathy were be examined by hematoxylin-eosin stain. The possible mechanisms affecting heat shock protein 70 (HSP70) and C-reactive protein (CRP) on nerves were studied by immunohistochemistry. The arsenic levels of the whole blood and the sciatic nerve were measured using Inductively Coupled Plasma Mass Spectrometry and correlated with the toxic effects on the peripheral nerve.

Results: After arsenic exposure, the hot stimulation latencies prolonged statistically significantly in arsenic exposure rats (37.60±1.77 vs. 5.60±1.50 seconds, $p<0.05$). The motor functions in terms of motion distance, velocity and spontaneous locomotion did not decrease significantly. The Na+/K+-ATPase and CRP activities of the sciatic nerve were inhibited, but the HSP70 activity was enhanced.

Conclusions: Chronic arsenic exposure could affect sensory nerve functions probably via enhancing HSP70 and inhibiting Na+/K+-ATPase and CRP activities.

key words, arsenic, peripheral neuropathy, heat shock protein 70, C-reactive protein, Na+/K+-ATPase